tral scotoma in both eyes. On the 6th day he was carried down to 4,700 m, but the following day he could walk unaided. By the 18th day, scotoma and impaired sensation disappeared, but his memory from the 3rd to the 5th day was lost. In February 1983 he was examined at our university hospital, and no abnormal findings were present in his optic fundi.

The symptoms of high altitude sickness have been well studied in the past.[2-5] At high altitude, mountaineers experience hypoxia, cold, hard exercise and, to a certain extent, malnutrition. In the two aforementioned cases, when they presented the symptoms the altitude was around 5,900 meters (converted to standard height) and the atmospheric pressure was about 50% of that at sea level.[6] The temperature several days prior to their illness ranged from 0°C to −10°C, but their clothes were sufficient to protect them against the cold. They engaged in activities under the same conditions as the other climbing members. Until up to two days before their symptoms developed, they had been taking meals as usual and also vitamin tablets every day. None of them had any remarkable past history of diseases involving peripheral nerves. In both cases, they noticed their impaired sensation for the first time only after they had regained consciousness. This fact led us to suspect that their symptoms appeared at the most crucial stage of high altitude sickness. These series of observations suggested that the causes of impaired sensory perception were related to hypoxia and some adjunctive factors. Locations and modalities of impaired sensation were identical with the ischaemic neuropathy caused by polycythaemia vera, namely, impaired perception of all sensory modalities in the distal extremities with preserved power in all muscle groups.[6]

At high altitude, marked polycythaemia more than $7 \times 10^6/mm^3$ could occur as the result of acclimatisation.[7] This polycythaemia can be excerbated by dehydration due to hyperventilation resulting in lowering circulation in the capillary system.[8] The transient nature of these polyneuropathic symptoms in our cases might be explained on the basis of ischaemia in the peripheral nerves.

KOUHEI ECHIZENYA
KUNIO TASHIRO
Division of Neurology,
Department of Neurosurgery,
University of Hokkaido,
School of Medicine,
North 15, West 7,
Kita-ku, Sapporo, 060,
Japan

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Matters arising

Polyneuritis cranialis in Lyme disease

Sir: It was interesting to read the article *Polyneuritis cranialis associated with Borrelia burgdorferi.*[1] We describe here a patient with bilateral facial palsy due to Lyme disease.

A 26-year-old man from the southern part of New Jersey state was admitted to hospital for left facial weakness of 2 days duration. Three weeks prior to this admission the patient had fever with chills for two days which subsided without any specific therapy. Subsequent to that he had bifrontal headaches and pain in the left mastoid region. Two days prior to the admission he developed numbness of the left side of mouth, tongue and the left eye. When he was seen in the hospital he had slight neck stiffness, dense lower motor neuron facial palsy and decreased facial sensation on the left side. A lumbar puncture was performed. The opening pressure was 12 cm of CSF. The protein was 41 mg/dl and sugar was 60 mg/dl. There were 169 WBC/mm^3; 95% were lymphocytes. Routine bacterial and fungal cultures were negative. A possibility of herpes encephalitis was considered. After 2 days he developed right lower motor neuron facial palsy. A CT scan of the head with and without contrast was normal. The antibodies titres to the Lyme disease spirochete were IgM 800 and IgG 400 units. The patient was not sure about any tick bite and he did not give any history of erythema chronicum migrans or arthritis. He was treated with 20 million units of penicillin G per day for 10 days with marked improvement in his headaches and some improvement of his facial palsy.

The patient described here did not have erythema chronicum migrans and arthritis and initially the diagnosis was in doubt. Erythema chronicum migrans occur in 89% of patients with Lyme disease with neurological complications. About 50% with neurological complications of Lyme disease have facial palsy and one-third of them have bilateral facial palsy.[2] Our patient had bilateral facial palsy and left V nerve involvement. In patients with multiple cranial nerve lesions even in the absence of erythema chronicum migrans and history of tick bite a possibility of Lyme disease should be considered before embarking on expensive and invasive diagnostic investigations. We agree with Schmutzhard *et al*, that Lyme disease is an important cause to be considered in the differential

diagnosis of polyneuritis cranialis.

PRATAP M YAGNIK
VITHAL DHADUK,
VA Medical Center,
Medical College of Pennsylvania,
Philadelphia, PA 19129,
USA

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Respiration and sleep in Parkinson's disease

Sir: We have read with great interest the recent paper by Apps *et al.*[1] on respiration and sleep in Parkinson's disease. We were particularly intrigued by the finding of an increase in respiratory rate among the Parkinson subjects compared with control subjects while awake and during REM sleep. It would be important to know if any direct measurement of minute ventilation or end tidal CO_2 was performed, that is, whether the tachypnoea was associated with true hyperventilation. Also, we wonder if their subjects had pulmonary function testing, as restrictive lung disease is often accompanied by increased respiratory frequency.

The authors appropriately point out that one possibility for this finding is an alteration of ventilatory control in Parkinson's disease. As there is a great deal of evidence that central catecholamines play a role in ventilatory drive,[2] this is a very reasonable speculation.

We have recently studied ventilatory drive in a group of 14 patients with Parkinson's disease (Hoehn and Yahr stages III–IV) and 11 age matched controls. All subjects had spirometry to rule out significant obstructive or restrictive lung disease. We did not observe changes in resting end tidal CO_2 or respiratory rate at rest in our group of Parkinson's patients. However, using rebreathing methods for hyperoxic hypercapnia and isocapnic hypoxia[3 4] we found an increased response in our Parkinson's disease subjects to both hypercapnia and hypoxia.[5] It is not yet clear whether this might be a central effect or whether dopamine metabolism in the carotid bodies of these patients is abnormal as well.

Further studies of ventilatory drive in Parkinson's disease should be of considerable interest both to expand our knowledge of this disease and to elucidate further the role of catecholamines in respiratory drive in man.

STEVEN H FEINSILVER
JOSEPH H FRIEDMAN
JONATHAN M ROSEN
Departments of Medicine and Neurology,
Brown University,
825 Chalkstone Avenue
Providence, RI 02908,
USA

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Apps replies:

I myself have carried out studies of hyperoxic hypercapnic rebreathing in Parkinsonian patients and found a normal response to this diminished breathing though some of the patients had an end tidal CO_2 at the lower end of the normal range.

Sensorimotor neuropathy and cisplatin and adriamycin toxicity

Sir: The brief report by Pages *et al*[1] of a severe sensorimotor neuropathy developing in a subject treated with adriamycin and cisplatin raises a number of interesting mechanistic questions. As they note, the occurrence though transient of a motor component to the neuropathy was unexpected and is as yet inexplicable. Neither of these drugs penetrates the normal blood-brain barrier[2] and this is shown by the low concentrations of cisplatin found in the CNS, although cisplatin may have access to peripheral nerve.[3] Both drugs must readily enter the spinal ganglia, presumably through fenestrations in the vascular bed noted some years ago.[4] Another possible route to motor nerves through their terminals is available,[5] but this is likely to be very minor by comparison, although with the very high dose of cisplatin given (about twice the amount usually considered to be neurotoxic) this route could conceivably have become more important.

The well known damage to sensory nerve fibres encountered in cisplatin intoxication is a different, and perhaps more straightforward, matter. The reduction in numbers of myelinated and unmyelinated axons in the sural nerve biopsy of this reported case confirms this and would be anticipated to be due to severe damage to their cell bodies within sensory ganglia, if our recent experimental studies in rats have any relevance to the matter.[6] While in this species it in fact has not been possible to reproduce the neuropathy, (for the animals die of non-neurological causes when the cumulative dose reaches only about 150 mg/m^2, which is about half the dose required to cause neuropathy in man), there is nevertheless unequivocal damage to nucleoli in a high proportion of sensory ganglion cells. This becomes visible within the first 24 hours of treatment with cisplatin and proceeds to segregation of the nucleolar constituents and later nucleolar fragmentation. Since nucleoli are the seat of ribosomal synthesis and nucleolar segregation is a sign of reduction or cessation of synthetic activity, it was not perhaps surprising to find that by the end of a week of treatment many ganglion cells showed severe reduction in Nissl material and conspicuous shrinkage of the whole cell. If the animals had not died from other causes, it is highly likely that cell death and/or axonal degeneration would have shortly followed, for these cellular events, while not precisely the same as those found with adriamycin in rat spinal ganglia, followed the same general sequence. Indeed, both drugs have somewhat analogous effects upon DNA and lead particularly to inhibition of RNA polymerase I activity,[7 8] the polymerase concerned with ribosomal transcription. In cisplatin toxicity ganglion cells are randomly affected regardless of size, and since small neurons responsible for unmyelinated and thinly myelinated fibres are substantially more numerous than large neurons concerned with the more discriminatory aspects of sensation, it is not wholly surprising that cases of neuropathy should occasionally show very little in the way of sensory loss of the latter type. The sural nerve biopsy showed in this case a substan-